

AMENDMENTS TO THE SPECIFICATION

In the specification:

Please enter the enclosed sequence listing on page 43 of the specification and renumber the pages with the Claims and Abstract accordingly. In addition to the diskette, a paper copy of the Sequence Listing is provided herewith.

Please amend the specification as shown:

Please delete the paragraph on page 2, lines 1-7, and replace it with the following paragraph:

--Many molecular derivatives of GLP-1 have been reported. For instance, GLP-1 (7-37) is known. A variety of analogs have also been described eg., Gln⁹-GLP-1 (7-37) (**SEQ ID NO: 15**), D-Gln⁹-GLP-1 (7-37), acetyl-Lys⁹-GLP-1 (7-37) (**SEQ ID NO: 16**), Thr¹⁶-Lys¹⁸-GLP-1(7-37) (**SEQ ID NO: 17**), and Lys¹⁸-GLP-1 (7-37) (**SEQ ID NO: 18**), Gly⁸-GLP-1 (7-37) (**SEQ ID NO: 19**), Ser⁸-GLP-1 (7-37) (**SEQ ID NO: 20**). Other GLP-1 derivatives (sometimes called "variants") have also been reported particularly as acid addition salts, carboxylate salts, lower alkyl esters, and amides. See WO 91/11457 and Mojssov, S., *Int. J. Peptide Protein Research*, 40:333-343 (1992), and references cites therein.--

Please delete the paragraph on page 10, lines 13-16, and replace it with the following paragraph:

--The amino acid sequence of GLP-1 (7-37) is well-known and has the following sequence: NH₂-His⁷-Ala-Glu-Gly¹⁰-Thr-Phe-Thr-Ser-Asp¹⁵-Val-Ser-Ser-Tyr-Leu²⁰-Glu-Gly-Gln-Ala-Ala²⁵²⁰-Lys-Glu-Phe-Ile-Ala³⁰-Trp-Leu-Val-Lys-Gly-Arg-Gly³⁷-COOH (**SEQ ID NO: 1**)--

Please delete the paragraph on page 10, lines 18-25, and replace it with the following paragraph:

--A "GLP-1 analog" is defined as a molecule having a modification including one or more amino acid substitutions, deletions, inversions, or additions when compared with GLP-1. GLP-1 analogs include, for example, GLP-1 (7-34) (SEQ ID NO: 21) and GLP-1 (7-35) (SEQ ID NO: 22), GLP-1 (7-36) (SEQ ID NO: 23), Val⁸-GLP-1 (7-37) (SEQ ID NO: 24), Gln⁹-GLP-1 (7-37) (SEQ ID NO: 15), D-Gln⁹-GLP-1 (7-37), Thr¹⁶-Lys¹⁸-GLP-1 (7-37) (SEQ ID NO: 17), and Lys¹⁸-GLP-1 (7-37) (SEQ ID NO: 18). Preferred GLP-1 analogs are GLP-1 (7-34) (SEQ ID NO: 21) and GLP-1 (7-35) (SEQ ID NO: 22), which are disclosed in U.S. Pat. No. 5,118,666, and also GLP-1 (7-36) (SEQ ID NO: 23). These compounds are the biologically processed forms of GLP-1 having insulinotropic properties. Other GLP-1 analogs are disclosed in U.S. Pat. No. 5,545,618.--

Please delete the paragraph on page 17, line 16, to page 18, line 12, and replace it with the following paragraph:

--More particular examples of GLP-1 and GLP-1 related molecules including analogs thereof such as those disclosed in the PCT/DK00/00393 application. Such molecules include the following specific compounds:

des Ser³⁹-exendin-4(1-39)-Lys₆-NH₂ (~~SEQ ID NO: 1~~);

des Pro³⁶-exendin-4(1-39)-Lys₆-NH₂ (~~SEQ ID NO: 2~~);

des Ala³⁵-exendin-4(1-39)-Lys₆-NH₂ (~~SEQ ID NO: 3~~);

des Gly³⁴-exendin-4(1-39)-Lys₆-NH₂ (~~SEQ ID NO: 4~~);

des Ser³⁹-(Lys⁴⁰ (palmitoyl))exendin-4(1-39)-Lys₇-NH₂ (~~SEQ ID NO: 5~~);

des Gly³⁴-(Lys⁴⁰ (palmitoyl))exendin-4(1-39)-Lys₇-NH₂ (~~SEQ ID NO: 6~~);

des Ala³⁵-(Lys⁴⁰ (palmitoyl))exendin-4(1-39)-Lys₇-NH₂ (~~SEQ ID NO: 7~~);

des Pro³⁶-(Lys⁴⁰ (palmitoyl))exendin-4(1-39)-Lys₇-NH₂ (~~SEQ ID NO: 8~~);

Lys⁴⁰ (palmitoyl)exendin-4(1-39)-Lys₇-NH₂ (~~SEQ ID NO: 1~~);
 des Pro³⁶, Pro³⁷ -exendin-4(1-39)-Lys₆-NH₂,
 Lys₆-des Pro³⁶, Pro³⁷, Pro³⁸ -exendin-4(1-39)-NH₂,
 Asn(Glu)₅-des Pro³⁶, Pro³⁷, Pro³⁸ -exendin-4(1-39)-NH₂,
 Lys₆-des Pro³⁶, Pro³⁷, Pro³⁸ -exendin-4(1-39)-Lys₆-NH₂
 Asn(Glu)₅-des Pro³⁶, Pro³⁷, Pro³⁸ -exendin-4(1-39)-Lys₆-NH₂,
 des Pro³⁶, Pro³⁷, Pro³⁸ -exendin-4(1-39)-Lys₆-NH₂,
 Gly⁸-GLP-1 (7-36)-Lys₆-NH₂ (SEQ ID NO: 6)
 Lys₆-Gly⁸-GLP-1 (7-36)-Lys₆-NH₂ (SEQ ID NO: 7),
 Lys₆-Gly⁸-GLP-1 (7-36)-NH₂ (SEQ ID NO: 8),
 (Gly⁸,Lys³⁷(palmitoyl)-GLP-1(7-36)(Human)-Lys₇-NH₂ (SEQ ID NO: 9),
 (Gly⁸,Lys²⁶(palmitoyl)-GLP-1(7-36)(Human)-Lys₆-NH₂ (SEQ ID NO: 10),
 (Gly⁸,Lys³⁴(palmitoyl)-GLP-1(7-36)(Human)-Lys₆-NH₂ (SEQ ID NO: 11),
 Gly⁸-GLP-1 (7-36)-Lys₈-NH₂ (SEQ ID NO: 12),
 Gly⁸-GLP-1 (7-36)-Lys₁₀-NH₂ (SEQ ID NO: 13),
 Gly⁸-GLP-1 (7-37)-Lys₆-NH₂ (SEQ ID NO: 14); and the free acid or pharmaceutically
 acceptable salt thereof.--

Please delete the paragraph on page 37, lines 12-19, and replace it with the following paragraph:

--*Insulin standard for quantitative PCR.* One µl first strand synthesis was used for PCR with the following insulin primers: 5'-AACCCACCCAGGCTTTTGTCA (SEQ ID NO: 2); 5'-CTTCCTCCACGTCCAGTTGTTC-3 (SEQ ID NO: 3). The amplicon were inserted into the PCR 4-TOPO vector (invitrogen) and transformed into E.coli. The plasmids were purified and 2 µg of each were linearized with either Spe I or Not I. The linearized plasmids were *in-vitro* transcribed using T7 or T3 RNA polymerase. After *in-vitro* transcription, the template was removed by DNase treatment. Subsequently, the mixture was phenol/chloroform-extracted and

precipitated. After precipitation the RNA was dissolved to 1 mg/ml in water.--

Please delete the paragraph on page 37, line 21, to page 38, line 3, and replace it with the following paragraph:

--*Quantitative PCR*. One μ g of both standard and sample were subjected to first strand synthesis as described above. A dilution series of the insulin mRNA standard, together with the samples were subjected to quantitative PCR using the following probe (Mouse insulin Taqman probe, 110-138) and the above described primers:

5'-FAM-AGGCTCTCTACCTGGTGTGTGGGGAGCGT-Tamra-3' **(SEQ ID NO: 4)**.

All PCR reactions were duplicates. The C_t (threshold cycle) were measured and the initial concentration of insulin mRNA was calculated according to the standard curve.

Drugs: COMPOUND 1 (H-HGEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAP PSKKKKKK-NH₂, **(SEQ ID NO: 5)** Batch: ZP15.65-3A) was produced at Zealand Pharma A/S using the Merifield technique.--